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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,844	02/01/2006	Dirk Beher	T1632Y	9399
210	7590	11/12/2008	EXAMINER	
MERCK AND CO., INC			RAO, SAVITHA M	
P O BOX 2000			ART UNIT	PAPER NUMBER
RAHWAY, NJ 07065-0907			1614	
			MAIL DATE	DELIVERY MODE
			11/12/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/566,844	BEHER ET AL.	
	Examiner	Art Unit	
	SAVITHA RAO	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 September 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 5-7,9 and 11-13 is/are pending in the application.
- 4a) Of the above claim(s) 11-13 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 5-7, 9 and 11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>02/01/2006</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 5-7, 9 and 11-13 are pending and are subject of this office action.

Claims 12-13 are withdrawn as being drawn to a non-elected invention and species

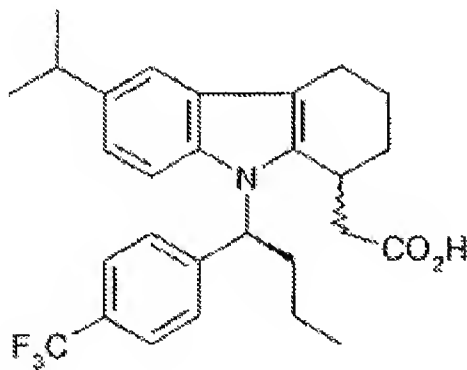
Claims 5-7, 9 and 11 are under consideration in the instant office action.

Election/Restrictions

Applicant's election of Group II (claims 5-7, 9 and 11 drawn towards a compound and a composition) without traverse in the reply filed on 09/10/2008 is acknowledged.

Application election of the following compound 'example 13' recited on page 55 of the specification is acknowledged

EXAMPLE 13



Claims 12-13 are withdrawn from consideration as being drawn to non-elected invention and specie.

Claims 5-7, 9 and 11 will be examined in the instant office action.

The Restriction requirement is therefore made final.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g)

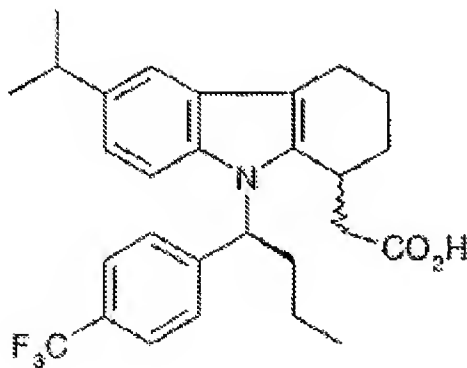
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prior art under 35 U.S.C. 103(a).

Claims 5-7, 9 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ford -Hutchinson (EP 0307077, referenced in instant IDS) as evidenced by Patani et al. (Chemical Reviews, 1996, vol. 96 (8), pages 3147-3176) in view of Watanabe (US 6,514,984)

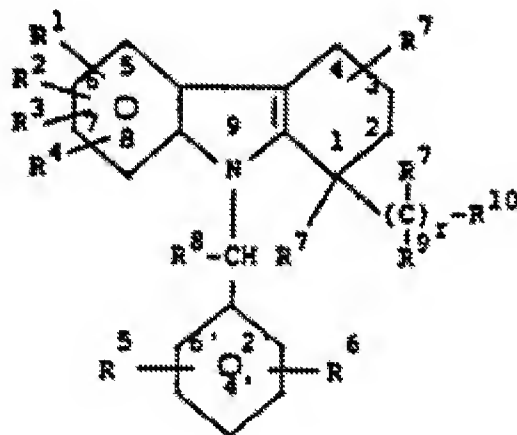
Instant claims are drawn towards the following compound (example 3)

EXAMPLE 13



Ford-Hutchinson teaches compounds of formula (I) shown below (page 4, lines 25-26 and claim 1). Among various substituents taught for each of the R variable below, the following listed substituent read on the instantly claimed compound

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I

Wherein R^1 = alkyl or alkenyl having 1-6 carbon atoms;

R^2 , R^3 and R^4 = H,

R^6 is $-(CH)_n M$ where $n = 0$ and M is CF_3

R^5 is H

R^7 is H

R^8 is H or alkyl of 1-6 carbon atoms

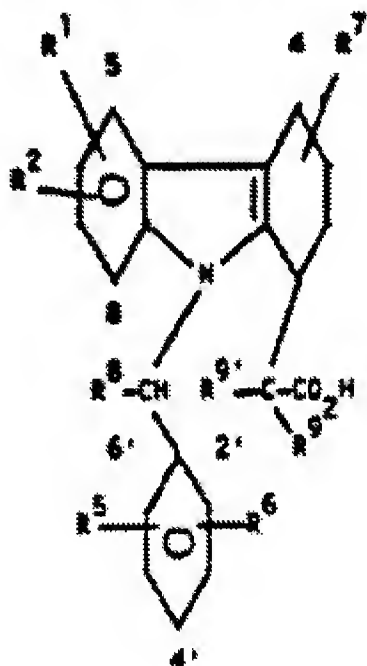
R^9 is H

R^{10} is $COOH$

Accordingly, the instantly claimed compound is entirely encompassed by the generic compound I taught by Ford- Hutchinson above

Ford-Hutchinson additionally teaches tetahydrocarbazole alkanolic acid compounds of general formula shown below (page 8, line 10-30 and page 10, lines 1 and 11)

Tetrahydrocarbazole
Alkanoic Acids



Compound	R ¹	R ²	R ³	R ⁴	R ⁸ , R ^{9'}	R ⁷	R ⁹
24 (Ex. 24)	6-CH(Me) ₂	H	4'-Cl	H	H, H	H	H

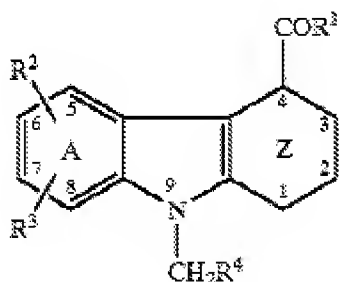
The only difference between the instantly claimed compound example 13 (page 55 of instant disclosure) and the compound taught by Ford-Hutchinson above are the substitution of 4' Chlorine instead of 4' trifluoromethyl group substitution in the position 4 of the N-CH₂-phenyl group and where R⁸ is H instead of propyl group of the instantly claimed compound. The generic formula teaches the substitution of CF₃ in position 4 of the N-CH₂-phenyl group and the substitution of alkyl group of 1-6 carbon at position R⁸.

Accordingly one of ordinary skill in the medicinal chemistry art would be motivated to synthesize the instantly claimed compound. Additionally, Patani et al is used here for evidence that the Cl group and CF₃ group are bioisosteres and one can be substituted by the other. Patani teaches that halogens have been replaced by electron-withdrawing groups such as a cyano or trifluoromethyl groups and illustrates such a nonclassical replacement of halogen in a structure activity relationship study of cholecystokin-A (CCK-A) receptor antagonists. CCK –A receptor antagonists have been proposed as potentially useful in the treatment of appetite disorders, abnormalities of gastric motility etc. As illustrated in Table 52 replacement of Cl with nonclassical bioisosteres such as CN or CF₃ resulted in retention of antagonistic activity at the CCK-A receptor (page 3172, section 6, Halogen Bioisosteres

Ford-Hutchinson does not teach the use of the compounds of his invention in a composition.

However, Watanabe teaches a method for the prevention and treatment of Alzheimer's disease by administering to a human in need thereof an effective amount of a substituted tricyclic secretory phospholipase A2 (sPLA2) inhibitor (abstract).

Watanabe teaches carbazole compounds of formula (XXX) below (col.10, lines 11-55)



(XXX)

Where R¹ is –NHNH₂ or –NH₂

R² is either hydroxy or alkoxy

R³ is H

R⁴ is –(C₁-C₄) alkyl phenyl

A is phenyl

Z is cyclohexenyl

Watanabe additionally teaches formulations comprising substituted tricyclic compounds of his invention which could be compositions suitable for internal administration together with a pharmaceutically acceptable diluent or carrier, the composition being adapted for the particular route of administration (col.55, lines 49-57).

Accordingly, it would have been *prima facie* obvious to the ordinarily skilled medicinal chemist to synthesize the instantly claimed compounds and compositions. Instantly claimed compound is encompassed by the generic compound taught by Ford-Hutchinson and Ford-Hutchison additionally teaches a compound structurally similar to the instantly claimed compound except for the chloro substitution instead of CF₃ and the H instead of Propyl group at the R₈ position of the compound taught by Ford-Hutchinson. Watanabe teaches structurally similar compounds useful for the treatment of Alzheimer's and teaches pharmaceutical compositions comprising them. Accordingly one of ordinary skill in medicinal chemistry art would be motivated to try out the range of substituents taught by Ford-Hutchinson to arrive at the instantly claimed compounds. Watanabe provides additional motivation as structurally similar compounds and compositions have been shown to be used for treatment of Alzheimer's disease. An

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ordinarily skilled artisan would be imbued with a reasonable expectation of success that compounds and compositions synthesized as taught by Ford-Hutchinson would find potential use for treatment of Alzheimers disease. It is to be noted that a prima facie case of obviousness may be made when chemical compounds have very close structural similarities and/or similar utilities. "An obviousness rejection based on similarity in chemical structure and/or function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties." In re Payne, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979). See In re Papesch, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) and In re Dillon, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1991).

Conclusion

Claims 5-7, 9 and 11 are rejected. No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAVITHA RAO whose telephone number is (571)270-5315. The examiner can normally be reached on Mon-Fri 7 am to 4 pm..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached at 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SAVITHA RAO/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614